89. (Amended) A method according to Claim 20, wherein the first quantity of injectable polarized gaseous $^{129}Xe$ is formulated for *in vivo* human administration.

90. (Amended) A method according to Claim 20, wherein the first quantity of injectable polarized gaseous $^{129}Xe$ is in a quantity less than about 5 cubic centimeters.

91. (Amended) A method according to Claim 20, further comprising evaluating the effectiveness of a therapeutic treatment based on the identifying step.

101. (Amended) A method according to Claim 20, wherein the obtaining step is commenced within about 5-25 seconds after the initiation of the injecting step.

## REMARKS

This Amendment is submitted in reply to the Official Action mailed December 23, 2002 ("the Action"). Claims 1, 3-23 and 89-102 are pending in the action.

### I. Allowable Subject Matter

Applicants acknowledge with appreciation the Examiner's statement that Claims 20, 21, 92, 93, 98 and 99 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 20 and 21 have been placed in independent form incorporating the subject matter of Claim 1. Please note that the preamble has been amended in a non-narrowing manner in each of these claims. Claims 92 and 93 depend directly or indirectly from Claim 20, and Claims 98 and 99 depend directly or indirectly from Claim 21. Hence, these claims are also in condition for allowance.

**II. Claims 22-23 and §103**

The Action rejects Claims 22 and 23 under §103 as being obvious over U.S. Patent No. 5,545,396 ("Albert et al.") alone and/or in view of U.S. Patent No. 5,811,076 ("Brasch") and further in view of U.S. Patent No. 6,315,981 ("Unger"). Applicants respectfully disagree.

The Action states that Claims 22-23 "are not limited to administering gas, by itself, but would encompass gas which [is] contained in some type of carrier, as disclosed by Unger." Action, p.4. Again, Applicants respectfully disagree.

However, Applicants have amended Claim 22 (Claim 23 depends from Claim 22) to substantially incorporate the subject matter of Claim 1, and to further recite in part:

> wherein the first quantity of polarized gaseous phase $^{129}Xe$ is formulated as a gaseous phase product with polarized $^{129}Xe$ as the primary injectable constituent, and wherein the gaseous phase polarized $^{129}Xe$ product is devoid of a liquid carrier constituent prior to injection.

Accordingly, as the Action implies that this feature renders these claims patentable at p. 4 of the Action as noted above, Applicants respectfully submit that Claims 22-23 are also in condition for allowance.

**III. Other Claims**

Applicants again note that they traverse the Action's characterization of the prior art and the obviousness rejections extended to the other pending claims. Indeed, Applicants believe that the claims as presented prior to the amendments herein are patentable over the cited art. However, in order to advance prosecution, Claim 1 has been cancelled above, without prejudice thereto, and Applicants have amended certain of the pending claims to depend from the amended allowable claims.

**IV. Conclusion**

A marked-up version of the amended claims is attached hereto. Applicants respectfully submit that the application is in condition for allowance which action is requested.

Respectfully submitted,

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**CERTIFICATE OF FACSIMILE TRANSMISSION**

I hereby certify that this correspondence is being sent by facsimile transmission to Box AF, Commissioner for Patents, Washington, DC 20231, at (703) 872-9307 on February 21, 2003.

Rosa Lee Brinson Date of Signature: February 21, 2003

**Marked-up Version of Claims**

3. (Amended) A method according to Claim [1] 20, further comprising the step of controlling the rate of injection to less than about 3 cc/s at which the injecting step is performed to thereby control the delivery rate of the polarized gaseous $^{129}Xe$ into the vein.

4. (Amended) A method according to Claim [2] 20, wherein said injected quantity is less than about 20 cc's.

5. (Amended) A method according to Claim [1] 20, wherein said identifying step includes determining based on said injecting into the vein step whether the pulmonary circulatory path is blocked or restricted based on the presence of polarized $^{129}Xe$ in the pulmonary arteries.

6. (Amended) A method according to Claim [1] 20, wherein said obtaining step includes obtaining NMR signal data associated with the presence of gaseous phase polarized $^{129}Xe$ in the lungs, the image signal intensity of which corresponds to the restriction, blockage or free passage of the pulmonary circulatory path.

8. (Amended) A method according to Claim [1] 20, further comprising the step of administering the injection such that the gaseous polarized $^{129}Xe$ substantially dissolves into the vasculature proximate to the injection site.

10. (Amended) A method according to Claim [1] 20, wherein said injecting step is carried out such that a major portion of the gaseous polarized $^{129}Xe$ remains substantially as a gas in the bloodstream and exhibits a $T_1$ in the bloodstream which is greater than about 8 seconds.

11. (Amended) A method according to Claim [1] 20, wherein said NMR signal data obtaining step is performed in a low magnetic field, wherein the field strength is less than

about 0.5T.

13. (Amended) A method according to Claim [1] 20, further comprising the step of introducing a second quantity of a polarized gas to a subject via inhalation during a single imaging session.

14. (Amended) A method according to Claim [1] 20, wherein said injection step is carried out intravenously.

18. (Amended) A method according to Claim [1] 20, wherein said injection comprises multiple sequential injections thereby allowing for multi-shot MR imaging.

20. (Twice Amended) [A method according to Claim 1, further comprising:]
A method of evaluating a subject, comprising the steps of:

positioning a subject having a pulmonary region and a blood circulation path including veins and arteries in an NMR system, the subject's pulmonary region having pulmonary veins and pulmonary arteries and associated vasculature defining a pulmonary portion of the circulation path;

injecting a first quantity of polarized gaseous phase $^{129}Xe$ directly into at least one vein of the subject, wherein the first quantity of polarized gaseous phase $^{129}Xe$ is less than about 100 cubic centimeters;

obtaining NMR signal data associated with the injected polarized $^{129}Xe$ in the pulmonary region of the subject, the signal data including information corresponding to the polarized gas introduced in said injecting step;

generating an MRI image having spatial visual representation of the NMR signal data of the injected polarized $^{129}Xe$;

identifying the presence of at least one condition of blockage, restriction, abnormality, and substantially unobstructed free passage of the pulmonary circulation path;

providing a container configured to hold the first injectable quantity of polarized

gaseous $^{129}Xe$ therein;

preparing the container to hold the first injectable quantity of polarized gaseous $^{129}Xe$ therein by introducing then expelling $CO_2$ from the container thereby leaving residual traces of $CO_2$ therein; and then

introducing the first quantity of polarized gaseous $^{129}Xe$ into the container prior to the step of injecting.

21. (Amended) [A method according to Claim 1, further comprising the step of]
A method for evaluating a subject, comprising the steps of:

positioning a subject having a pulmonary region and a blood circulation path including veins and arteries in an NMR system, the subject's pulmonary region having pulmonary veins and pulmonary arteries and associated vasculature defining a pulmonary portion of the circulation path;

injecting a first quantity of polarized gaseous phase $^{129}Xe$ directly into at least one vein of the subject, wherein the first quantity of polarized gaseous phase $^{129}Xe$ is less than about 100 cubic centimeters;

obtaining NMR signal data associated with the injected polarized $^{129}Xe$ in the pulmonary region of the subject, the signal data including information corresponding to the polarized gas introduced in said injecting step;

generating an MRI image having spatial visual representation of the NMR signal data of the injected polarized $^{129}Xe$;

identifying the presence of at least one condition of blockage, restriction, abnormality, and substantially unobstructed free passage of the pulmonary circulation path; and

introducing a quantity of surfactant into a subject proximate to the injection site of the $^{129}Xe$.

22. (Amended) [A method according to Claim 1, further comprising the step of]
A method of evaluating a subject, comprising the steps of:

positioning a subject having a pulmonary region and a blood circulation path

including veins and arteries in an NMR system, the subject's pulmonary region having pulmonary veins and pulmonary arteries and associated vasculature defining a pulmonary portion of the circulation path;

injecting a first quantity of polarized gaseous phase $^{129}Xe$ directly into at least one vein of the subject, wherein the first quantity of polarized gaseous phase $^{129}Xe$ is less than about 100 cubic centimeters, wherein the first quantity of polarized gaseous phase $^{129}Xe$ is formulated as a gaseous phase product with $^{129}Xe$ being the primary constituent and devoid of liquid carrier components prior to injection;

obtaining NMR signal data associated with the injected polarized $^{129}Xe$ in the pulmonary region of the subject, the signal data including information corresponding to the polarized gas introduced in said injecting step;

generating an MRI image having spatial visual representation of the NMR signal data of the injected polarized $^{129}Xe$;

identifying the presence of at least one condition of blockage, restriction, abnormality, and substantially unobstructed free passage of the pulmonary circulation path; and

expelling the $^{129}Xe$ gas from a container into the subject during said injecting step such that the formation of large $^{129}Xe$ gas bubbles are inhibited during said injecting step.

89. (Amended) A method according to Claim [1] 20, wherein the first quantity of injectable polarized gaseous $^{129}Xe$ is formulated for *in vivo* human administration.

90. (Amended) A method according to Claim [1] 20, wherein the first quantity of injectable polarized gaseous $^{129}Xe$ is in a quantity less than about 5 cubic centimeters.

91. (Amended) A method according to Claim [1] 20, further comprising evaluating the effectiveness of a therapeutic treatment based on the identifying step.

101. (Amended) A method according to Claim [1] 20, wherein the obtaining step is commenced within about 5-25 seconds after the initiation of the injecting step.